ORIGINAL RESEARCH ARTICLE

Development of a technology for producing medicated lozenges with carbon dioxide extracts of Acorus calamus L. rhizomes and Calendula officinalis L. flowers

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Volume 1 · Issue 2 · 2026 · e0006 · Published: 8 October 2026 · Version of Record

Abstract

Introduction. Medicated lozenges are solid unit-dose dosage forms intended to dissolve slowly in the oral cavity and pharynx, thereby providing prolonged contact of active components with the mucosa. The incorporation of plant extracts into medicated lozenges is of interest in the development of locally acting products; in this context, particular importance is attached to establishing process parameters that provide a stable technological mass and enable its subsequent moulding.

Objective. To develop a technology for producing medicated lozenges containing carbon dioxide extracts of Acorus calamus L. rhizomes and Calendula officinalis L. flowers.

Materials and methods. Thick carbon dioxide extracts of Acorus calamus L. rhizomes (batch AC 0103.2024) and Calendula officinalis L. flowers (batch CO 0103.2024), manufactured by PLP Zhanafarm LLP, were used as the plant components. The excipients were sugar, isomalt, glucose syrup, glycerol, citric acid, food colour and purified water. The laboratory process comprised preparation of the starting components, preparation of the base under heating and mixing, incorporation of the plant extracts, production of a homogeneous mass, cooling and casting into moulds. Dosing accuracy, operation temperature and duration, residual moisture, mass homogeneity and moulding parameters were monitored.

Results. The working ranges of the principal process parameters were established: 135–140 °C for preparation of the carbohydrate base, 115–120 °C for glycerol incorporation, 80–85 °C for incorporation of the carbon dioxide extracts, 15–25 rpm for mixing and 15–20 min at 5 °C for cooling. When residual moisture of the lozenge mass was reduced to approximately 1%, the technological properties required for casting were achieved. The mass of one lozenge was 0.6 g. The sequence of the main operations and the parameters to be controlled were specified.

Conclusion. A laboratory technology was developed for producing medicated lozenges containing carbon dioxide extracts of Acorus calamus L. rhizomes and Calendula officinalis L. flowers on a sugar-isomalt base with glucose syrup. Working ranges were established experimentally for preparation of the carbohydrate base, incorporation of glycerol and plant extracts, mixing, moulding and cooling. The findings provide a basis for a laboratory process scheme and may be used in developing a manufacturing procedure for the lozenges.

Keywords: medicated lozenges; Acorus calamus L.; Calendula officinalis L.; carbon dioxide extracts; isomalt; manufacturing technology; in-process control

To cite this article: Ibadullayeva G.S.. Development of a technology for producing medicated lozenges with carbon dioxide extracts of Acorus calamus L. rhizomes and Calendula officinalis L. flowers. Pharmaceutical Sciences and Health Products. 2026;1(2):e0006.

Introduction

Oral diseases remain highly prevalent and constitute a major medical and social problem. According to the World Health Organization, approximately 3.5 billion people, or about 45% of the world population, are affected by oral diseases [1]. This high burden supports the development of dosage forms for local application in the oral cavity that are convenient to use and provide prolonged contact of active substances with the mucosa.

Medicated lozenges are among the dosage forms intended for local action in the oral cavity and pharynx. The Pharmacopoeia of the Eurasian Economic Union defines medicated lozenges as solid unit-dose forms produced by casting or compression, containing one or more active substances uniformly distributed in an appropriate base and intended to dissolve in the mouth to exert a local effect [2]. Carbohydrate components are commonly used as the base for cast lozenges, and the lozenge mass may be prepared at 90–140 °C [2].

Plant-derived substances are one direction of pharmaceutical development for locally acting dosage forms. This study used carbon dioxide extracts of Acorus calamus L. rhizomes and Calendula officinalis L. flowers. Calendula officinalis L. flowers are described in a European Medicines Agency monograph as herbal material used,

among other indications, in conditions of the mouth and throat [3]. Current evidence for Acorus calamus L. indicates a complex composition of rhizome constituents, including essential-oil components, terpenoids and phenylpropanoids; anti-inflammatory and antimicrobial properties have been reported experimentally [4].

The production of medicated lozenges containing plant substances requires justification of the sequence of operations and of the time-temperature parameters, particularly during preparation of the carbohydrate base and incorporation of the extracts. Recent studies of herbal medicated lozenges confirm that process parameters are important for achieving the required characteristics of the finished dosage form [5].

The aim of this study was to develop a technology for producing medicated lozenges containing carbon dioxide extracts of Acorus calamus L. rhizomes and Calendula officinalis L. flowers.

Materials and methods

Thick carbon dioxide extracts of Acorus calamus L. rhizomes (batch AC 0103.2024) and Calendula officinalis L. flowers (batch CO 0103.2024), manufactured by PLP Zhanafarm LLP, were used as the plant components. Sugar, isomalt, glucose syrup, glycerol, citric acid and food colour were used as excipients (Table 1).

Table 1. Composition of medicated lozenges containing carbon dioxide extracts of Acorus calamus L. and Calendula officinalis L.

Component	Content, %	Functional purpose
Carbon dioxide extract of Acorus calamus L. rhizomes	0.2	Plant-derived active component
Carbon dioxide extract of Calendula officinalis L. flowers	0.2	Plant-derived active component
Sugar	28.0	Carbohydrate-matrix former and sweetener
Isomalt	30.0	Base-forming component, sweetener and structuring agent
Glucose syrup	40.0	Sweetener and matrix component; promotes formation of a homogeneous mass
Glycerol	0.7	Plasticizer and humectant
Citric acid	0.8	Acidity regulator and flavour modifier
Food colour	0.1	Colouring agent; provides the required organoleptic characteristics
Total	100.0	

The laboratory process comprised raw-material preparation, preparation of the carbohydrate base, incorporation of glucose syrup, glycerol and plant extracts, moulding, cooling and primary packaging.

Stage 1 - raw-material preparation. The specified amounts of carbon dioxide extracts, isomalt, sugar, glucose syrup, glycerol, citric acid and food colour were weighed on laboratory balances. Starting materials underwent incoming quality control.

Stage 2 - preparation of the carbohydrate base. Isomalt and sugar were heated with continuous stirring to 140 °C. The mixing rate was maintained at 20–25 rpm until a homogeneous carbohydrate base was obtained.

Stage 3 - incorporation of glucose syrup. The specified amount of glucose syrup was added to the carbohydrate base and heating was continued under constant mixing. The operation continued until a homogeneous lozenge mass with approximately 1% residual moisture was obtained.

Stage 4 - incorporation of glycerol. After the high-temperature stage, the lozenge mass was cooled to 120 °C. Glycerol was incorporated and the mass was mixed until the component was distributed uniformly and a homogeneous consistency was achieved.

Stage 5 - incorporation of active and thermolabile ingredients. The mass was further cooled to 80 °C. The carbon dioxide extracts, citric acid and food colour were added and mixed at 20–25 rpm until homogeneous.

Stage 6 - moulding. The prepared mass was dispensed into pre-prepared moulds by casting. The mass of one lozenge was 0.6 g. Uniformity of dosing, individual mass, shape and appearance were monitored.

Stage 7 - cooling and setting. The moulded lozenges were cooled at 5 °C for 15 min until setting was complete, then removed from the moulds.

Stage 8 - primary packaging. After finished-product control, the lozenges were individually packaged and sent for labelling.

Equipment. Laboratory manufacture used an enamelled vessel, an electric hotplate with adjustable heating, a thermometer for the technological mass, laboratory balances and lozenge moulds.

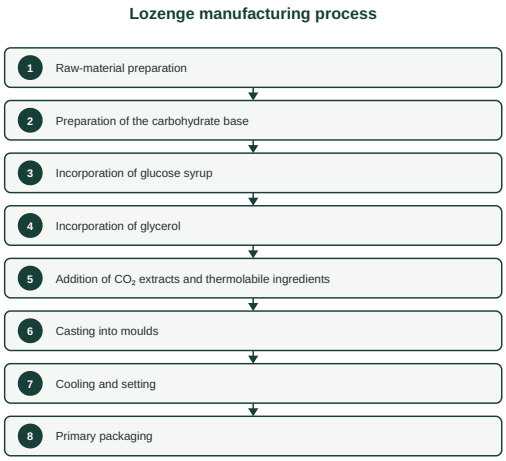


Figure 1. Process scheme for producing medicated lozenges containing carbon dioxide extracts of Acorus calamus L. and Calendula officinalis L.

Results

The experimental development investigated the influence of the principal process parameters on the characteristics of the lozenge mass and formation of the finished dosage form.

The variables included the temperature used to prepare the carbohydrate base, the temperatures of glycerol and extract incorporation, mixing rate and cooling time. Technological acceptability was evaluated by homogeneity and flow, uniform distribution of components, presence of air inclusions, mouldability, degree of setting and preservation of lozenge integrity after removal from the moulds.

Table 2. Experimental evaluation of the process parameters

Parameter	Value	Assessment criteria	Actual result / observation	Assessment
Carbohydrate-base preparation temperature, °C	135	Homogeneity, flow, residual moisture, colour change	The mass met the adopted technological criteria	Acceptable
Carbohydrate-base preparation temperature, °C	140	Homogeneity, flow, residual moisture, colour change	The mass met the adopted technological criteria	Acceptable
Carbohydrate-base preparation temperature, °C	145	Homogeneity, flow, residual moisture, colour change	More intense darkening indicated excessive thermal exposure	Unacceptable
Glycerol-incorporation temperature, °C	115	Distribution, consistency, air inclusions	Glycerol was distributed uniformly; consistency remained acceptable	Acceptable
Glycerol-incorporation temperature, °C	120	Distribution, consistency, air inclusions	Glycerol was distributed uniformly; consistency remained acceptable	Acceptable
Glycerol-incorporation temperature, °C	125	Distribution, consistency, air inclusions	Intensive bubbling hindered production of a homogeneous mass	Unacceptable
Extract-incorporation temperature, °C	85	Flow, uniform distribution, mouldability	The mass retained sufficient flow; extracts were distributed uniformly	Acceptable
Extract-incorporation temperature, °C	80	Flow, uniform distribution, mouldability	The mass retained sufficient flow; extracts were distributed uniformly	Acceptable
Extract-incorporation temperature, °C	95	Flow, uniform distribution, organoleptic properties	Organoleptic characteristics changed	Unacceptable
Mixing rate, rpm	15	Distribution, air inclusions, flow	Uniform distribution and acceptable flow	Acceptable
Mixing rate, rpm	20	Distribution, air inclusions, flow	Uniform distribution and acceptable flow	Acceptable
Mixing rate, rpm	25	Distribution, air inclusions, flow	Uniform distribution and acceptable flow	Acceptable
Cooling at 5 °C, min	10	Setting, demoulding, integrity	Setting was incomplete; shape retention was insufficient	Unacceptable
Cooling at 5 °C, min	15	Setting, demoulding, integrity	Adequate setting; the lozenges retained their shape	Acceptable
Cooling at 5 °C, min	20	Setting, demoulding, integrity	Adequate setting; the lozenges	Acceptable

Parameter	Value	Assessment criteria	Actual result / observation	Assessment
			retained their shape	

Preparation of the carbohydrate base at 135–140 °C provided acceptable characteristics. Heating to 145 °C caused more intense darkening and was excluded from the subsequent process.

Incorporation of glycerol at 115–120 °C provided uniform distribution. At 125 °C, intensive bubble formation hindered production of a homogeneous mass.

The technologically acceptable range for incorporation of the carbon dioxide extracts was 80–85 °C; at this temperature the mass remained sufficiently fluid and the extracts were distributed uniformly. At 95 °C, changes in organoleptic characteristics were observed.

Within the tested mixing range of 15–25 rpm, a homogeneous mass with the required flow characteristics was obtained.

Cooling at 5 °C for 10 min was insufficient for complete setting. Cooling for 15–20 min provided adequate setting and preservation of shape and integrity after removal from the moulds.

Discussion

The results confirm that the technological characteristics of medicated lozenges are determined not only by the composition of the carbohydrate base but also by the sequence of operations and the thermal regime. For plant-containing lozenges, process control is particularly important because a homogeneous amorphous carbohydrate matrix must be formed while thermal exposure of plant components is limited. Butkevych et al. similarly used separate temperature stages and incorporated plant extracts after cooling the mass to 80 °C [6].

The working range of 135–140 °C is consistent with known patterns in the thermal processing of concentrated carbohydrate systems. At 145 °C, more pronounced darkening indicated a greater thermal load. The exact processing temperature depends on composition; therefore, the range established here should be considered specific to the developed formulation [7,8].

The carbohydrate base contains sugar, isomalt and glucose syrup. Structural and mechanical properties of amorphous isomalt systems depend on water content and the presence of other carbohydrate components; increased moisture lowers the glass-transition temperature and increases the risk of stickiness and structural instability [9]. Glucose syrup contributes to formation of an amorphous matrix and limits sucrose crystallization.

The experimentally established glycerol-incorporation range of 115–120 °C provided homogeneity, whereas intensive bubbling occurred at 125 °C. Directly comparable data for an identical sugar-isomalt lozenge composition were not identified; this parameter should therefore be regarded as process-specific.

Incorporation of the carbon dioxide extracts at 80–85 °C preserved flow and enabled uniform distribution, whereas organoleptic changes were observed at 95 °C. This range agrees with a published process in which plant extracts were added after the lozenge mass had been cooled to 80 °C [6].

The low-temperature nature of CO_2 extraction provides an additional rationale for adding the extracts after preliminary cooling [10]. The present observations do not establish whether the composition of biologically active substances changed; that question requires additional chemical and analytical studies.

Mixing at 15–25 rpm provided uniform component distribution without meaningful differences according to the technological criteria used. Establishing a working range rather than a single set point is valuable for later scale-up and is consistent with modern pharmaceutical-development principles [5].

Cooling time was also important. Ten minutes at 5 °C was insufficient, whereas 15–20 min produced lozenges that retained shape and integrity. The molten high-viscosity mass must pass into a stable glassy state; cooling parameters therefore affect setting, deformation and subsequent stability [11].

Conclusion

The experimental work established acceptable operating ranges of 135–140 °C for preparation of the carbohydrate base, 115–120 °C for glycerol incorporation, 80–85 °C for addition of the carbon dioxide extracts, 15–25 rpm for mixing, and 15–20 min at 5 °C for cooling and setting. Stepwise temperature reduction allows the auxiliary and plant components to be incorporated before moulding. These ranges can be used in developing a manufacturing procedure.

Funding

The study received no external funding.

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